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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/538,976	12/05/2005	Seetharama A. Acharya	96700/1023	6788
1912 7590 02/07/2008 AMSTER, ROTHSTEIN & EBENSTEIN LLP 90 PARK AVENUE NEW YORK, NY 10016			EXAMINER LIU, SAMUEL W	
			ART UNIT 1656	PAPER NUMBER
			MAIL DATE 02/07/2008	DELIVERY MODE PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary

Application No.

10/538,976

Applicant(s)

ACHARYA ET AL.

Examiner

Samuel W. Liu

Art Unit

1656

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 21 November 2007.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 8-21 and 28 is/are pending in the application.
- 4a) Of the above claim(s) none is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 8-21 and 28 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 21 November 2007 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)
Paper No(s)/Mail Date <u>12/21/07 & 11/21/07</u> . | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Status of claims

Claims 8-21 and 28 are pending.

The amendment filed 11/21/07 which amends claims 8 and 19-2, cancels claims 1-7, and adds claim 28 has been entered. New claim 28 is drawn to elected invention; and thus, claims 8-21 and 28 are examined in this office action.

Withdrawal of the Objections/rejections

- The objection to the Spec is withdrawn in light of the amendment to the Spec thereof.
- The objection to claims 1-27 is withdrawn in light of the cancellation of claims 1-7 and 22-27, and in light of the amendment to claim 8.
- The rejection of claims 7 and 19-21 under 35 USC 112, second paragraph, is withdrawn in light of the cancellation of claims 1-7.
- The rejection of claims 1-27 under 35 USC 102, is withdrawn in light of the cancellation of claims 1-7 and 22-27, and in light of the applicants submission of declaration under 37 CFR 1.131 which indicates that prior to the January 11, 2003 priority date (102(e) date) of Winskow et al. (US Pat. No. 6974795 B2), Applicants had reduced the claimed method to practice. Said "declaration" therefore overcomes the rejection thereof.
- The rejections under 35USC of (i) claims 1-7 by Acharya et al. (US Pat. No. 6017943), and (ii) of claims 1-7 by Acharya et al. (US Pat. No. 7144989 B2), are withdrawn in light of the cancellation of claims 1-7.

IDS

The references cited in the IDS filed 12/21/07 and the IDS filed 11/21/07 have been considered by Examiner.

* Examiner note: the Spec has full support for the subject matter of new claim 28 “ HB has six \pm one PRG chain” (see paragraph [0021]).

New-Objections to Claim 28

Claim 28 is objected to because, for consistence, “HB” should be changed to "Hb" (see claim 21).

New-Claim Rejections - 35 USC §102

Claim Rejections - 35 USC §102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless -

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 8-21 and 28 are rejected under 35 U.S.C. 102(b) as being anticipated by Acharya et al. (US Pat. No. 6017943).

At col. 7, line 64 to col. 8, line 26, Acharya et al. teach preparation of polyethylene glycol (PEG) modified hemoglobin (Hb) which comprises the steps: (i) reacting Hb with a thiolating agent, e.g., iminothiolane, and (ii) reacting with the thiolated “Hb” with the “PEG compound”

which is produced by conjugation with a compound containing maleimide moiety, e.g., 4-(or 3-)-phenylmaleimido (col. 8, line 4 and Examples 5-6).

Acharya et al. teach that, in step (i), the thiolation of "Hb" is carried out under the reaction condition that the thiolating agent is about 5-20 fold molar excess over the concentration of Hb (col. 8, lines 7-10); this meets the limitation of claim 8, step (a).

Acharya et al. teach that, in step (ii), PEGlation of the thiolated Hb is performed under the reaction condition that the thiolated "Hb" concentration is 0.1 mM-3.0 mM (col. 5, line 4), and, the concentration of the "PEG compound" (having formula of "Ic", see col. 5, line 48), i.e., the maleimidized PEG, is about 6.0 mM to 200 mM (0.2. M). Given that the thiolated "Hb" concentration is about 3.0 mM, then, the maleimidized PEG is about 2-66 fold excess over of the thiolated "Hb". This is obvious variation of the reaction condition of claim 8, step (b).

Therefore, Acharya et al. teach the process of claim 8.

"Thiolating agent is about 5-20 fold molar excess over the concentration of Hb" taught by Acharya et al. is an obvious variation of the instant "9-12 fold excess" recited in claim 9, and an obvious variation of the instant "about 10 fold excess" recited in claim 10. Thus, claims 9-10 are included in the rejection.

The range "about 2-66 fold excess" taught by Acharya et al. encompasses/reads on the maleimidized PEG concentrations of "about 18-22 fold excess" (claim 11) and "about 20 fold excess" (claim 12), which anticipates claims 11-12. Similarly, the reaction condition taught by Acharya et al. with regard to the maleimidized PEG concentration range teaches the maleimidized PEG concentration of instant claims 11 and 12.

In Figure 6, and col. 3, lines 23-25, Acharya et al. teach that the "PEG compound", i.e., "Mal-PEG 5000", wherein "Mal" refers to maleimimidyl group (see col. 4, lines 1-2), which anticipates claim 17-18.

Since the non-hypertensive is an inherent property of the PEGylated Hb (see the discussion at page 4, 7th paragraph, the Office action mailed 7/27/07), the above Acharya et al. teachings anticipate claims 19-21.

Claim 28 is directed to the end-product produced by the claimed method. Because the claimed method is anticipated by the prior art teaching (see above), the product thereof should be also anticipated.

Conclusion

No claims are allowed.

Discussion of the art

The art made of record and not currently relied upon in any rejections is considered pertinent to Applicants' disclosure:

- Application 11919788 (788), which has common inventive entity to instant application, discloses a method (claims 17-36) of preparing PEGylated Hb comprising conjugating a maleimide PEG to a thiol group of a Cys residue of Hb. 788 is not considered to be the reference for provisional obviousness type double patenting because the pending claims of 788 do not disclose the instant two steps (claim 8): reacting Hb with 8-15 fold excess of a thiolation agent, e.g., iminothiolane, subsequently followed by reacting the thiolated Hb with 16-30 excess of maleimide PEG.

• Application 11921064 (064), which has common inventive entity to instant application, discloses a method (claims 27-36) of preparing PEGylated Hb comprising (i) reacting Hb with a thiolation agent; and (ii) reacting the thiolated Hb with a PEGylating agent, e.g., maleimide modified PEG (claim 31). 064 is not considered to be the reference for provisional obviousness type double patenting because the claims of 064 do not disclose the reaction conditions recited in instant claim 8, i.e., reacting Hb with 8-15 fold excess of a thiolation agent (e.g., iminothiolane), and subsequently reacting the thiolated Hb with 16-30 excess of the maleimidized PEG; wherein "8-15 excess fold" and "16-30 excess fold" are considered to be a part of the essential subject matter of the claimed process of claims 8-21 and 28 of instant application. Thus, claims 27-36 of 064 are not considered to be obvious variation of instant claim 8 or/and dependent claims therefrom.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Samuel Wei Liu whose telephone number is 571-272-0949. The examiner can normally be reached from 9:00 a.m. to 5:30 p.m. on weekdays. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor Kathleen Kerr Bragdon can be reached on 571-272-0931. The fax phone number for the organization where this application or proceeding is assigned is 703 308-4242 or 703 872-9306 (official) or 703 872-9307 (after final). Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703 305-4700.



Samuel Wei Liu, Ph.D.
Patent Examiner, Art Unit 1656
January 28, 2008



KAREN COCHRANE CARLSON, PH.D
PRIMARY EXAMINER